46 cases in which the diagnosis was determined with only cytology, 9 cases were different in diagnosis between cytology and pathology. Seven cases were different only in cell typing of primary lung cancer. One case diagnosed as primary lung cancer by cytology was diagnosed as metastatic lung cancer from colon cancer by pathology. The other case diagnosed as metastatic lung cancer from breast cancer was diagnosed as primary lung cancer by pathology. There were no false positive cases regarding malignancy.

Conclusion: These results suggest that intra-operative FNA cytology with the modified Shorr's staining method is useful for diagnosing malignancy-suspected pulmonary nodules in clinical practice.

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Multicentric phase II trial of Cisplatin plus Etoposide chemotherapy in advanced Large-Cell Neuro Endocrine Carcinoma of the Lung (LCNEC): preliminary results. Study 03-02 from the "Groupe Francais de Pneumo-cancerologie" (GFPC)

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Introduction: A few prospective studies concerning diagnosis and treatment of large cell neuroendocrine lung cancer were published, as this tumor seems relatively rare. The objectives of GFPC 03-02 prospective study were to establish the efficiency of Cisplatinum /Etoposide chemotherapy and to valid value of large spectrum cytokeratins in the diagnosis of neuro-endocrine differnciation.

Methods: Patients with stage IV and stage III B (with neoplasic pleural effusion) were included; treatment consisted in three cycles of Cisplatinum 80mg/m^2 d1 / Etoposide 100mg/m^2 d1d2d3 and two more cycles in case of objective response or stable disease.

The primary objective is the efficiency of this chemotherapy, secondary objective the validation of the paranuclear granular expression of a large spectrum cytokeratin, as a characteristic of neuro-endocrine differentiation. Slides were controlled by a panel of pathologists. Diagnoses were based on Travis's criterias.

Results: 27 patients were included since May 2004. The slides of 21 cases were reviewed. 14 cases were confirmed as LCNEC. 4 were excluded on the basis of the nuclear criteria or cell size, and classified as small-cell carcinomas (SCC). One was excluded, because immunohistochemistry was not available. Two other patients were excluded because of the misinterpretation of the pathologic report by the clinicians (one SCC, one Large cell Carcinoma).

Among the 14 cases, two sub-types were observed:

- 8 LCNEC with neuroendocrine features and positive immunohistochemistry
- 6 undifferentiated carcinomas with immunohistochemical neuroendocrine differentiation.

None case was diagnosed as large-cell carcinoma with neuroendocrine pattern and negative immunohistochemistry.

Table 1. Immunohistochemical results

Antibodies	Positive	Negative	Not Evaluated
Cytokeratin (AE1/AE3 or KL1 or MNF116)	5	2	7
Chromogranin A	12	0	2
Synaptophysin	12	0	2
CD56	6	3	5
TTF1	7	2	5

In all cases, at least two of the three neuroendocrine markers (chromogranin A, synaptophysin, CD56) were positive.

Discussion: Interobserver variability is not observed on the criterias of neuroendocrine immunohistochemical differentiaton, but only on the criterias of size. Some small scratched samples led to difficulties to distinguish small-cell carcinoma from large-cell carcinoma, especially when neuroendocrine morphology (rosettes, trabecular growth pattern,…) was not present. It seems necessary to definite how many of the Travis's criterias are necessary to accept the diagnosis of LCNEC (cell size, chromatin, nucleoli, nuclear-to-cytoplasmic ratio, large and eosinophilic or granular cytoplasm) when neuroendocrine differentiation is proved. This interobserver variability is described in the literature (1).

Value of the paranuclear granular expression with Cytokeratins must be evaluated on cases not yet tested.

Conclusion: Panel of pathologists is useful to diagnose LCNEC. Disagrements were on cell size, some LCNEC were reclassified as SCC. Usefulness of cytokeratins needs some more patients tested.

(1) W.D.Travis, A.A. Gal, T.V. Colby and coll. Reproductibility of neuroendocrine lung tumor classification. Hum Pathol 1998, 29: 272-279

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Subepithelial myofibroblast in lung adenocarcinoma: immonohistochemical characterization and prognostic significance

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Stromal invasion of cancer is associated with proliferation of stromal myofibroblasts. These cells are considered as activated fibroblasts that facilitate invasion and metastasis of cancer cells. Myofibroblasts in early lung adenocarcinoma lesions, such as pure bronchiolo-alveolar carcinoma (BAC) and mixed type adenocarcinoma with a BAC component, are not well documented in the literature. We report here the presence of subepithelial myofibroblasts in pure bronchiolo-alveolar carcinoma (BAC) and a subset of invasive lung adenocarcinomas. We also characterized their immunohistochemical profiles, investigated their relationships with stromal invasion and the prognostic significance.

Materials and Methods: A total of 75 cases of surgically resected lung adenocarcinomas were examined. There were 9 cases of BAC, 14 cases of mixed type adenocarcinoma with a BAC component, and 52 cases of pure invasive adenocarcinomas. All cases were immunostained for smooth muscle α-actin to visualize myofibroblasts. Selected cases were also stained for calponin, desmin and h-caldesmon.

Results: In all cases of pure BACs, we could observe subepithelial myofibroblasts. These cells were characterized by their peculiar location between cancer cells and alveolar septa. Immunohistochemically, they were positive for smooth muscle α-actin and calponin. Some were